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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/866,569 | 05/25/2001 | Anthony E. Bolton | 033136-185 | 4479 |

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| EXAMINER | |
|---|---|
| YAEN, CHRISTOPHER H | |
| ART UNIT | PAPER NUMBER |
| 1643 | |

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/866,569 | BOLTON ET AL. | |
| | Examiner | Art Unit | |
| | Christopher H. Yaen | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/12/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

**Re: BOLTON *et al***

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 12/12/2005 has been entered.

2. Claims 1-15 are canceled without prejudice or disclaimer

3. Claims 16-29 are pending and examined on the merits.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Information Disclosure Statement*

5. The Information Disclosure Statement filed 12/12/2005 is acknowledged and considered. A signed copy of the IDS is attached hereto.

### *New Rejections*

### *Claim Rejections - 35 USC § 112, 1st paragraph*

6. Claims 16-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are drawn to a method of treating congestive heart failure (CHF) comprising the administration of apoptotic bodies to a mammal affected with said disease. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001). The claims encompass the treatment of CHF comprising the administration of apoptotic bodies to a patient affected by CHF.

The art teaches that CHF is a disease associated with an elevated level of pro-inflammatory cytokines, such as TNF-alpha, which have been linked to the pathogenesis and progression of the disease. The art also teaches that in patients with CHF, the levels of IL-10 (a well known marker for TH2 responses or anti-inflammatory cytokine) and its receptor are increased (see Yamaoka et al Jpn Circ J. 1999;

63(12):951-956*)*. The art also teaches that in patients with CHF, there appears to be an imbalance in the Th1/Th2 cytokine profile, wherein there tends to more of a TH1 type response (i.e. inflammatory response - see Aukrust *et al* Ann. Med. 2005;37:74-85). The art also teaches that treatments to modulate such cytokines profiles have been difficult and challenging (see page 81 Aukrust *et al*).

The specification of the instant application provides a single working example wherein a mouse model for contact hypersensitivity or CHS (an example of a Th1 type disorder) is used to show that upon administration of the apoptotic bodies, there was a decreased amount of inflammation (see page 16, for example). The specification then indicates that based on the CHS model, that the reduction in inflammation would indicate that Th2 cytokines (i.e. anti-inflammatory cyokines) have been elevated such that the balance between Th1 and Th2 have been restored (see page 17, for example).

The specification fails to provide a sufficient nexus between the administration of apoptotic bodies in the CHS model and the treatment of CHF. The specification does not provide any profiles of inflammatory cytokines in the CHS model and fails to show that Th2 or anti-inflammatory cytokines are elevated such that it would alleviate any disease, much less treat CHF as claimed. Moreover, given the general state of the art regarding the modulation of Th1/Th2 cytokines, one of skill in the art would require additional guidance in the form of a working example that show the treatment of CHF, wherein the administration of apoptotic bodies altered the Th2 immune response as indicated. Applicant have not provided sufficient evidence in the specification as filed that the apoptotic bodies are in any way associated with the modulation of cytokines.

Instead what the application has show is that the administration of the apoptotic bodies reduced the swelling and or thickness an ear in a mouse.

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of the efficacy of the control and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CHRISTOPHER YAEN
PATENT EXAMINER

Christopher Yaen, Examiner
Art Unit 1643
March 8, 2006